Page 2 [Amendment Under 37 C.F.R. §1.116 to the July 18, 2000 Office Action - January 18, 2001]

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TECH CENTER 1600/2900

KINDLY AMEND THE ABOVE-IDENTIFIED APPLICATION AS FOLLOWS:

In The Title of the Invention:

Change the title of the invention to

-- Oligo- or Polydeoxyribonucleotides and Oligo- or Polynucleotides

Comprising Phosphate Moiety Non-Radioactively Labeled

Modified Nucleotides -- .

In The Claims:

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11) 3

Please amend claims 454, 455, 459, 461, 466, 476, 480, 482, 483, 487, 489, 494, 504, 508, 510, 511, 512, 513, 514, 515, 516, 517, 518, 519, 520, 521, 522, 523, 524, 525, 526, 527, 528, 529, 530, 531, 533, 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, 554, 555, 556, 557, 558, 559, 561, 563, 564, 565, 566 and 567 as follows:

454. (Amended) An oligo- or polydeoxynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxynucleotide comprising at least one modified nucleotide having the formula

Sig-PM-SM-BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a base moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM, said BASE being attached to SM, and Sig being covalently attached to PM directly or through a chemical linkage, said Sig [being a moiety capable non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

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455. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein said Sig is or renders the nucleotide or the oligo- or polydeoxyribonucleotide self-signaling or self-indicating or self-detecting.

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459. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] α -position relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

461. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] $\underline{\alpha}$ position relative to the point of attachment to the nucleotide, or any of the moieties:

$$- CH = CH_{2} - NH -$$

$$- CH = CH - CH_{2} - NH -$$

$$[- CH = CH - CH_{2} - O - CH_{2} - CH - NH -,$$

$$OH,]$$

$$- CH = CH - CH_{2} - O - CH_{2} - CH - CH_{2} - NH -,$$

$$OH,$$

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466. (Amended) The oligo- or polydeoxyribonucleotide of claim 454, wherein Sig

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is selected from the group consisting of a ligand and a specific ligand binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

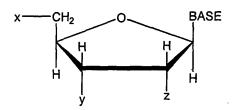
Me

476. (Amended) The composition of claim 474, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin.

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480. (Amended) The oligo- or polydeoxyribonucleotide of claim 478, wherein the sugar moiety of said terminal nucleotide has [hydrogen] oxygen atoms at each of the 2' and 3' positions thereof.

482. (Amended) An oligo- or polydeoxyribonucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polydeoxyribonucleotide comprising at least one modified nucleotide having the structural formula:



wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H- , HO- , a monophosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H-, HO-, a monophosphate, a di-phosphate and a tri-phosphate;

wherein z is <u>selected from the group consisting of H</u>—, <u>HO—, a monophosphate</u>, a di-phosphate and a tri-phosphate; and

wherein Sig is covalently attached [to x, y or z] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y, z, and a combination thereof, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to [x, y or z] said phosphate or when said modified nucleotide is incorporated into said oligo- or polydeoxynucleotide or when said oligo- or polydeoxynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof.

Claim 483, line 2, after "oligo or" and before "self-signaling" change "polynucleotide" to -- polydeoxyribonucleotide -- .

MID

mil

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487. (Amended) The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] α-position relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

489. (Amended) The oligo- or polydeoxyribonucleotide of claim 482, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] $\underline{\alpha}$ -position relative to x, y or z, or any of the moieties:

0 || - S -, - C - O, and - 0 - .

494. (Amended) The oligo- or polydeoxyribonucleotide of claim 482, wherein Sig is selected from the group consisting of a ligand and a specific ligand binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

504. (Amended) The composition of claim 502, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin.

508. (Twice Amended) The oligo- or polydeoxyribonucleotide of claim 506, wherein both y and z of said terminal nucleotide comprise [a hydrogen] an oxygen atom at each of the 3' and 2' positions thereof, respectively.

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510. (Amended) The oligo- or polydexoyribonucleotide of claim 482, having the structural formula:

, wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

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511. (Amended) An oligo- or [polyribonucleotide] <u>polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide</u> comprising at least one [ribonucleotide] <u>modified nucleotide</u> having the formula

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, said PM being attached to SM [at a position of SM selected from the 2', 3' and 5' positions, or combinations thereof], said BASE being attached to SM, and Sig being covalently attached to PM directly or via a chemical linkage, said Sig [being a moiety capable of non-radioactive detection] comprising a nonradioactive label moiety which can be directly or indirectly detected when attached to PM or when said modified nucleotide is incorporated into said oligo- or [polyribonucleotide] polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide, and when Sig is attached through a chemical linkage to a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not [a cleaved 3' terminal ribonucleotide] obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said [oligo- or polyribonucleotide] oligoribonucleotide or polyribonucleotide.

512. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein said Sig is or renders the nucleotide <u>or the oligo- or polynucleotide</u> self-signaling or self-indicating or self-detecting.

Claim 513, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 514, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 515, line 1, change "polyribonucleotide" to -- polynucleotide -- .

516. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] <u>α-position</u> relative to the point of attachment to the nucleotide, a -CH₂NH- moiety, or both.

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Claim 517, line 1, change "polyribonucleotide" to -- polynucleotide -- .

518. The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein said chemical linkage comprises or includes an olefinic bond at the [delta-position] α <u>position</u> relative to the point of attachment to the nucleotide, or any of the moieties:

$$- CH = CH_{2} - NH -$$

$$- CH = CH - CH_{2} - NH -$$

$$[- CH = CH - CH_{2} - O - CH_{2} - CH - NH -,$$

$$OH,$$

$$]$$

$$- CH = CH - CH_{2} - O - CH_{2} - CH - CH_{2} - NH -,$$

$$OH,$$

0 || *-* S *-* , *-* C *-* O, and *-* 0 *-* .

Claim 519, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 520, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 521, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 522, line 1, change "polyribonucleotide" to -- polynucleotide -- .

523. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein Sig is <u>selected from the group consisting of a ligand and a specific ligand</u>

binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin].

Claim 524, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 525, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 526, line 1, change "polyribonucleotide" to -- polynucleotide -- .

mn

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Claim 527, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 528, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 529, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 530, lines 1 and 2, change "polyribonucleotide" to -- polynucleotide -- .

Claim 531, line 1, change "polyribonucleotide" to -- polynucleotide -- .

533. (Amended) The composition of claim 531, wherein said polypeptide is selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin.

535. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 511, wherein said Sig moiety is attached to a terminal [ribonucleotide] <u>nucleotide</u> in said oligo- or [polyribonucleotide] <u>polynucleotide</u>.

536. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 535, wherein the sugar moiety of said terminal [ribonucleotide] <u>nucleotide</u> has a hydrogen atom at the 2' position thereof.

537. (Amended) The oligo- or [polyribonucleotide] <u>polynucleotide</u> of claim 535, wherein the sugar moiety of said terminal nucleotide has [a hydrogen] <u>an oxygen</u> atom at each of the 2' and 3' positions thereof.

Claim 538, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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539. (Amended) An oligo- or [polyribonucleotide] <u>polynucleotide which is complementary to a nucleic acid of interest or a portion thereof, said oligo- or polynucleotide</u> comprising at least one <u>modified</u> nucleotide having the structural formula:

wherein BASE is a moiety selected from the group consisting of a pyrimidine, a purine and a deazapurine, or analog thereof, and wherein BASE is attached to the 1' position of the pentose ring from the N1 position when BASE is a pyrimidine or from the N9 position when BASE is a purine or a deazapurine;

wherein x is selected from the group consisting of H- , HO- , a monophosphate, a di-phosphate and a tri-phosphate;

wherein y is selected from the group consisting of H-, HO-, a monophosphate, a di-phosphate and a tri-phosphate;

wherein z is selected from the group consisting of H-, HO-, a mono-phosphate, a di-phosphate and a tri-phosphate; and

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wherein Sig is covalently attached [to x, y or z] directly or through a chemical linkage to at least one phosphate selected from the group consisting of x, y and z, and a combination thereof, said Sig [being a moiety capable of non-radioactive detection] comprising a non-radioactive label moiety which can be directly or indirectly detected when so attached to [x, y or z] said phosphate or when said modified nucleotide is incorporated into said oligo- or polynucleotide, or when said oligo- or polynucleotide is hybridized to said complementary nucleic acid of interest or a portion thereof, provided that when said oligo- or polynucleotide is an oligoribonucleotide or a polyribonucleotide and when Sig is attached through a chemical linkage to [y of] a terminal PM at the 3' position of a terminal ribonucleotide, said chemical linkage is not [a cleaved 3' terminal ribonucleotide] obtained through a 2',3' vicinal oxidation of a 3' terminal ribonucleotide previously attached to said [oligo- or polyribonucleotide] oligoribonucleotide or polyribonucleotide.

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Claim 540, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 541, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 542, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 543, line 1, change "polyribonucleotide" to -- polynucleotide -- .

544. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 539, wherein said chemical linkage comprises a member selected from the group consisting of an olefinic bond at the [alpha-position] a-position relative to the point of attachment to the nucleotide, a -CH2NH- moiety, or both.

Claim 545, line 1, change "polyribonucleotide" to -- polynucleotide -- .

546. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 539, wherein said chemical linkage comprises or includes an olefinic bond at the [deltaposition] α -position relative to x, y or z, or any of the moieties:

$$- CH = CH_{2} - NH -$$

$$- CH = CH - CH_{2} - NH -$$

$$[- CH = CH - CH_{2} - O - CH_{2} - CH - NH -,$$

$$OH,$$

$$OH,$$

$$]$$

$$- CH = CH - CH_{2} - O - CH_{2} - CH - CH_{2} - NH -,$$

$$OH,$$

| | - S -, - C - O, and - O - .

Claim 547, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 548, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 549, line 1, change "polyribonucleotide" to -- polynucleotide -- .

Claim 550, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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551. (Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 539, wherein Sig is selected from the group consisting of a ligand and a specific ligand M23 binding protein [complexed with a binding protein therefor, and said binding protein is conjugated to ferritin]. Claim 552, line 1, change "polyribonucleotide" to -- polynucleotide -- . Claim 553, line 1, change "polyribonucleotide" to -- polynucleotide -- . Claim 554, line 1, change "polyribonucleotide" to -- polynucleotide -- . Claim 555, line 1, change "polyribonucleotide" to -- polynucleotide -- . Claim 556, line 1, change "polyribonucleotide" to -- polynucleotide -- . Claim 557, line 1, change "polyribonucleotide" to -- polynucleotide -- . Claim 558, lines 1 and 2, change "polyribonucleotide" to -- polynucleotide -- in both instances. Claim 559, line 1, change "polyribonucleotide" to -- polynucleotide -- . 561. (Amended) The composition of claim 559, wherein said polypeptide is MZY selected from the group consisting of avidin, streptavidin and [anti-Sig] anti-hapten immunoglobulin. Claim 563, lines 1 and 2, charge "polyribonucleotide" to -- polynucleotide -- , both instances. Claim 564, line 1, change "polyribonucleotide" to -- polynucleotide -- . 565. (Twice Amended) The oligo- or [polyribonucleotide] polynucleotide of claim 563, wherein both y and z of said terminal nucleotide comprise [a hydrogen] an oxygen atom at each of the 3' and 2' positions thereof, respectively.

Claim 566, line 1, change "polyribonucleotide" to -- polynucleotide -- .

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567. (Amended) The oligo- or [polydexoyribonucleotide] <u>polynucleotide</u> of claim 539, having the structural formula:

, wherein m and n represent integers from 0 up to about 100,000, and wherein said Sig moiety is attached to at least one of the phosphate moieties in said structural formula.

Cancel claims 568-575.